REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 71-106 are in the application subsequent to entry of this Amendment.

Claim 106 has been added considering the examiner's comments in item 2 of the Official Action of August 13, 2007.

The balance of the Official Action deals with two separate rejections of the claims, claims 71-105 (all of the claims) are rejected in item 4 of the Official Action based on a combination of four documents while claims 79-105 are rejected in item 5 of the Official Action based on a combination of two documents. The claims now pending include claims 71-85 and 94-106 directed to methods while the remaining claims are directed to compositions.

The Official Action makes no distinction between the two types of claims, namely the considerations as to patentability for the composition claims are quite different from the criteria for assessing patentability of the method claims. In particular, method claims do not require novel compositions but, in fact, are directed to obtaining a certain goal or objective and the means to obtain that goal or objective, namely the composition, does not require applicants to demonstrate that the composition itself is novel or inventive but rather that the objective of the method is novel and inventive considering the overall content of the involved claim(s).

It is applicants' position that at the very least the method claims are distinguishable from various combinations of the prior art (as set forth in the Official Action) and that they define novel and inventive procedures. Moreover, it would appear the documents have been illogically combined to construct the two prior art-based rejections given in items 4 and 5 of the Official Action in that the combination of documents does not arrive at the claimed subject matter and in fact certain combinations would not produce a viable product/workable result. This is explained in more detail in the remarks that follow. During previous examination applicants have already revised their claims and directed them to preferred taxol and camptothecin derivatives following the formula given in the involved claims. As to the cosmetically active substance used in the methods of claims 79 and 106, for example, the active ingredient is not disclosed in the prior art.

Wang in Combination with Allen

Wang et al solve the problem of DNA delivery in gene therapy by providing a liposome made of a number of esters of L-carnitine which efficiently complex with DNA. No suggestion is given in Wang to use this liposome to deliver drugs.

US 6,056,973 (Allen) discloses liposome composition comprising: a liposome made of cationic lipids (other than L-carnitine derivative or esters) and conjugates. The conjugates are made of a lipid (having a lipophilic head and a hydrophilic tail) linked to a hydrophilic polymer and to a targeting ligand. An active agent is entrapped in the liposome (camptothecins are included). These long circulating liposomes having a targeting ligand (usually an antibody) solves the problem of providing a liposome composition which provides flexibility in choice of the entrapped agent and the targeting ligand. According to Allen et al., the hydrophilic polymer and the targeting ligand are essential features for drug delivery.

Allen et al do not disclose esters of L-carnitine/acyl L-carnitine-made liposome which entrap taxol or camptothecin.

The object of the present invention is to provide a new liposome that is stable and highly selective in reaching the target organ. The technical problem is solved by the compounds of formula (I) (esters of L-carnitine)and (II) (acyl L-carnitine).

The content of these two references may be accurately summarized as follows: Wang teaches that esters of L-carnitine-made liposomes are useful only for gene delivery. Allen teaches that, in order to deliver drugs, such as camptothecin, the liposome must be a complex made of liposome+conjugated hydrophilic polymer and the targeting ligand.

A person of ordinary skill in the art, with the problem of selective delivery of camptothecins and taxol to target organs, using Wang et al as starting point, would not have found in Allen et al any useful direction to the presently claimed invention. In fact, there is no disclosure in Allen et al that carnitine and its esters are suitable for making liposomes for selective delivery of camptothecins and taxol. Further, there is no indication in Allen et al that the liposome, deprived of its conjugation with hydrophilic polymer and the targeting ligand would work in any effective way for drug delivery. In fact, Allen teaches just the opposite.

Therefore, the skilled person would not have arrived at the present invention, by combining the cited references, because this person should have taken a Wang et al liposome and

try to use it for selective delivery to target organ of camptothecins and taxol without conjugating it with hydrophilic polymer and the targeting ligand, thus contravening the requirements of Allen et al.

A skilled person must follow all of the teachings of the prior art not just "convenient" portions (as in the Action) and does not have the freedom to modify the prior art unless there is a clear indication to do so with the expectation of success.

This rejection is based on selective reading of Allen and as such it is incorrect. Fairly combining the full teachings of both references would result in an unworkable/ineffective product.

Accordingly, the claimed invention is patentable with respect to the cited references. Withdrawal of rejection is respectfully requested.

Wang in Combination with Burke

Wang was previously discussed. Wang refers to gene delivery only. There is no indication that carnitine-based liposomes can stabilize molecules completely different from nucleic acids.

US 5,552,156 (Burke) overcomes the problems of insolubility and instability of camptothecin drugs administered in their free form by providing that the lactone of the camptothecin structure is intercalated in the bilayer of a liposome so that the ring is protected from hydrolysis. The liposome is made of phosphatidylcholine, phosphatidylglycerol and mixtures thereof, distearoylphosphatidylcholine, and dimystoylphosphatidilglycerol.

Burke does not disclose esters of L-carnitine/acyl L-carnitine-made liposome and does not suggest that L-carnitine/acyl L-carnitine in a liposome can act as a stabilizer of taxol or camptothecin and allowing its selective delivery to a target organ.

The person skilled in this art would not obtain the solution of the present application by combining Wang with Burke since Burke lists which lipids (other than carnitine) positively effect camptothecin delivery.

The skilled person would not be burdened to transfer the knowledge provided by Wang et al. in the field of gene delivery to the field of camptothecin and taxol delivery as both the means and objectives are entirely different.

In fact, the skilled person would find that Allen et al provide an exhaustive list of cationic lipids for making liposomes for drug delivery (camptothecin included). Very strangely, Allen never cites the possibility of using carnitine and its esters as cationic lipid for the same scope.

The only use provided by the art for carnitine and its esters for making liposomes is for gene delivery as taught by Wang.

Burke goes in an opposite direction from Allen, since the liposomes are made by neutral or negatively charged lipids (column 6, lines 16-34). Therefore, Burke cannot be combined with Wang or Allen, since he departs from their specific teaching and would never arrive at the presently claimed invention. Accordingly, the claimed invention is patentable with respect to the cited references. Withdrawal of rejection is respectfully requested.

Wang in Combination with Stracher

Wang was previously discussed, and the same arguments pertain and are not repeated but still relied on.

Stracher US 5,008,288 discloses a carrier (liposome) selected from carnitine and cysteic acid covalently bonded through an alcohol, carboxyl or amine group to a pharmaceutically active compound selected from the group consisting of pepstatin, procainamide, quinidine, propranolol and leucyl arginina. Stracher does not disclose liposome made of esters of L-carnitine and acyl L-carnitine of formula (I) and (II), respectively.

In Stracher L-carnitine is only taught to be the selective carrier for a drug specific to cardiac and skeletal muscle and no indication is given that an ester of an alkanoyl L-carnitine can be employed to prepare a cationic liposome for selective delivery to target organs for antitumor drugs such as camptothecins and taxol.

Thus, by combining the teachings of the two documents, one relating to gene delivery and the other relating to cardiovascular disease treatment, the skilled person would not obtain what is presently claimed, specific for the field of antitumor drugs. Moreover, the skilled person will learn that carnitine liposomes as taught by Wang are specific for gene delivery, and these liposomes are not contemplated by Allen and Burke, who deal with antitumor drugs. Accordingly, the claimed invention is patentable with respect to the cited references. Withdrawal of rejection is respectfully requested.

Wang in Combination with Hsu

Wang was previously discussed, the same arguments pertain herein and are not repeated but still relied on.

Hsu US 5,653,996 is a general disclosure relating to liposomes which can be made by phospholipids, a mixture of phospholipids, polar lipids, neutral lipids, fatty acids, and their derivatives. Preferred are the ester, alcohol, and acid forms of stearate, oleic acid, linoleic acid, arachidate, arachidonic acid, and other single-aliphatic chains acids, ester, alcohol, and acid forms of the retinols, in particular, retinol and retinoic acid. Particularly preferred lipids include phosphatidylcholine (PC), phosphatidylglycerol (PG) and their derivatives. These lipsomes can be used for delivering active ingredients.

Hsu does not specifically disclose an L-carnitine/acyl L-carnitine-made liposome for the selective delivery of taxol or camptothecin.

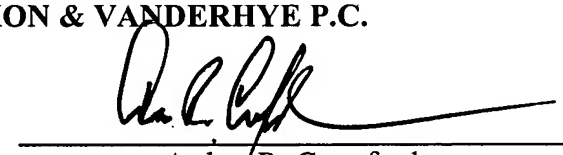
Considering the combination of Wang and Hsu, one of ordinary skill in the art would not prepare L-carnitine/acyl L-carnitine-made liposomes containing taxol or camptothecin.

The skilled person would not find any useful information in the above cited references, since Wang, as previously said specifically teaches gene delivery only. In view of the above, applicants submit that claims 71-85 and 94-106 are inventive over the prior art and allowance of the application is respectfully awaited.

For the above reasons it is respectfully submitted that the claims of this application define inventive subject matter. Reconsideration and allowance are solicited.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

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